JOURNAL AMERICAN DENTAL SOCIETY OF ANESTHESIOLOGY, INC.

VOLUME XII • NUMBER 4 • APRIL 1965

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The **Journal** is published monthly, except during June-July and August-September, when it is published bi-monthly, by the American Dental Society of Anesthesiology, Inc.

Subscription to the **Journal** is $2.50 and is included in the annual membership dues of the Society. Address all applications to Dr. Richard I. Weaver, 500 Toledo Medical Building, Toledo 2, Ohio.

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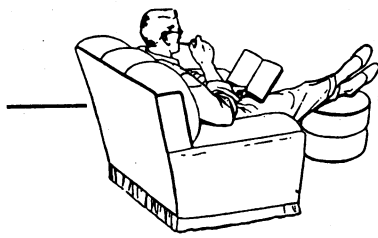
Member of the American Association of Dental Editors.

Second Class Postage has been paid at Brooklyn, N. Y.

Scientific Abstracts



Articles in this section are selected by Drs. Richard Lowell, Donald Wallace, Darryl Pirok, and Alan Miller

Therapeutic Efficacy of Antidepressant Drugs

Cole, Jonathan O.
J. Amer. Med. Assoc. 190:488-455, 1964

The place of the newer antidepressant drugs in the physician's armamentarium is not yet clear, but many clinicians feel that the drugs are useful and effective.

Careful controlled clinical studies have not always led to unequivocally positive findings. Even when the findings have been favorable to a drug under study, the differences between it and the placebo have not been as great as desirable or as anticipated from uncontrolled studies.

Two reasons probably account for this. First, depression is one of the psychiatric conditions that have a favorable prognosis for eventual recovery with or without treatment. Second, depression has been described as a symptom, as a syndrome, and as a disease. The entity being treated with a new antidepressant drug varies so greatly that response to the drug can be expected to vary widely. Furthermore, the state is treated with non-drug therapy, electroconvulsive therapy, as well.

Current concern about certain antidepressant drugs results from their widespread use in general practice. Since the drugs are potent pharmacologic agents, the concern may be justified.

The antidepressants may be conveniently classified into two groups, those like imipramine and the monoamine oxidase inhibitors. The imipramine group includes imipramine and amitriptyline, currently available, and others now being studied. In normal individuals, imipramine acts like a sedative if a single dose is given. In severely depressed subjects, striking improvement is seen a day or two after treatment is begun. The effective dose reported ranges from 150 to 350 mg. per day. Comparative studies indicate that where the drug is effective at all, it is more effective than placebo, comparable to tranylcypromine, and less effective than electroconvulsive therapy.

Monoamine oxidase inhibitors include phenelzine, nialamide, isocarboxazid, pargyline, and tranylcypromine. Ipromiazid, pheniprazine, and etryptazine have been withdrawn from commerce.

There are almost no sound studies which correlate actual inhibition of

monoamine oxidase with clinical change in depressed patients being treated with these agents. Clinical judgments also differ concerning the efficacy of the drugs. Some of the confusion rests on uncertainty about the effective dose level. The drugs may have different effects on brain enzymes than on peripheral or liver enzymes. Significant pharmacologic effects apart from, or independent of, monoamine oxidase may be found.

The question of why patients may respond to only one of the group of drugs is yet unanswered.

Safety and toxicity problems associated with monoamine oxidase inhibitors were illustrated when iproniazid, now withdrawn, was associated with a number of patients with severe hepatic necrosis. The monoamine oxidase inhibitors also produce unwanted interactions. This suggests that the imipramine class of drugs should be used first in depressed patients.

Adverse Reactions to Phenothiazines

Hollister, Leo E.
J. Amer. Med Assoc. 189:311-313, July 27, 1964

Although commonly held to be clinically useful in the treatment of emotional disorders, phenothiazine derivatives are classic examples of the fact that few drugs have only one effect. These drugs have medical importance as antiemetic agents and as adjuncts to anesthetic and analgesic drugs. Some of the phenothiazine derivatives have been found useful as antihistaminics, and some have anticholinergic adrenergic blocking, or metabolic-endocrine actions.

This wide range of pharmacodynamic actions contributes to the variety of adverse reactions the phenothiazine derivatives may evoke. Adverse behavioral effects are sometimes observed. As a rule, the more seriously disturbed the patient, the better his tolerance for the drug. Mildly affected patients tolerate small doses well. An unusual characteristic of the drugs is that it is virtually impossible to commit suicide with these drugs as sole agents. Clinical addiction is unknown.

Phenothiazines produce several uncommon central nervous system reactions. Extrapyramidal syndromes depend most on the individual's susceptibility; other factors include the patient's age and sex and the dose of the drug.

A syndrome resembling parkinsonism has been observed; dystonic syndromes occur more frequently in children and young adults.

Autonomic nervous system effects, primarily due to adrenergic blockade or anticholinergic actions, are more common to older patients. Allergic or toxic reactions have been reported, and are similar to those caused by other agents. Cholestatic jaundice occurs in fewer than 0.5 per cent of the patients. Agranulocytosis occurs less frequently.

Metabolic and endocrine effects attributable to phenothiazine drugs in-

clude weight gain, which may be countered by appropriate diet; edema, which is self-limiting and usually disappears; lactation, gynecomastia, and menstrual irregularities, which require that the attending physician only reassure the patient, and increased libido in women and impotency in men, which require the same treatment.

Miscellaneous effects reported as side effects of phenothiazine administration include hypostatic pneumonia, trophic ulcers, local inflammation, gangrene, electrocardiographic abnormalities, potentiation of other drugs and alcohol, teratogenic effects, pigmentary retinopathy, melanin pigmentation, and corneal and lens deposits.

If phenothiazine derivatives were not so valuable in clinical practice, this list of undesirable side effects would have caused them to be removed from the market. Fortunately, most of the side effects occur early in treatment and are easily recognized. The drugs must be used carefully, and never for trivial purposes.

Pentazocine — A New Nonaddicting Analgesic

Sadove, Max; Balagot, Reuben C., and Pecora, Faustino N.
J. Amer. Med. Assoc. 189:199-202, July 20, 1964

The search for a clinically acceptable, nonaddicting, potent analgesic has been carried out in many laboratories and clinics for decades. Using novel structure-activity relationships, based on analgesic antagonists, a new drug, pentazocine, Win 20,228, was developed.

A preliminary single-blind study, involving 185 male postoperative patients, was used to evaluate the analgesic effectiveness of the drug. Pentazocine was given postoperatively to a group of patients selected at random, one-half to five hours after their arrival in the recovery room. All patients were awake and complaining of pain. The dose given ranged from 20 to 40 mg. Only one dose was given.

In terms of analgesic effectiveness, pain relief was good. One hundred seventy-six patients had reduced pain scores after drug administration. Onset of relief was rapid, usually within 20 minutes. Duration of relief was as long as three hours in more than half the patients. Duration was related to the amount of drug given.

Sedation was found in some patients within 20 minutes after drug administration; maximum drowsiness occurred later. This effect was seen in most of the patients. Other side effects included blood pressure changes, nausea, vomiting, euphoria, slurred speech, dizziness, headache, and tremors. These effects were rare, and most of those listed occurred only once in the series.

Respiratory changes included depression of respiratory rate, which occurred at all dose levels and lasted for several hours. The depression was not sufficient to prevent unaided compensation and did not appear to be a problem. Hallucinogenic and other psychic effects were absent.

Hemodynamic Effects of External Cardiac Compression

MacKenzie, G. J.; Taylor, S. H.; McDonald, A. H., and Donald, K. W.
Lancet 1:1342-1345, 1964

The purpose of cardiac massage is to produce adequate perfusion of vital tissues with oxygenated blood. That external cardiac compression can produce this effect appears to be justified from the numerous reports which have appeared since 1960.

Three patients were studied after cardiac arrest. The systemic arterial pressure, the right atrial pressure, and the cardiac output of the patients was measured during spontaneous heart activity and during external cardiac compression.

During spontaneous activity the blood pressure and cardiac output were reduced in association with elevated right atrial pressure. During external cardiac compression, satisfactory systolic arterial pressure was produced, but cardiac output was further reduced. Compression produced large systolic venous pressure pulses of an amplitude similar to the arterial pulse.

Accepting systolic pressure pulses as indicative of forward blood flow is fallacious. The pulse recorded is a pressure pulse, and is not indicative of blood flow. Much of the pulse recorded is due to direct transmission of extra-thoracic compression applied directly to the aorta.

These findings indicate that internal cardiac massage should be reconsidered. If cardiac massage needs to be continued for more than a brief period, the external technic would seem to be less efficient than internal massage.

Citanest: A New Local Anesthetic Agent

Sadove, Max S.; Rosenberg, Ronald; Heller, Floyd N.; Stortz, Michael J., and Albrecht, Ronald F.
Anesthesia & Analgesia 43:527-532, 1964

Searches for local anesthetic agents chemically of high potency and low toxicity have led to the development of propitocaine (α-*n*-propylamino-2-methylpropionanilide) (Citanest). This drug is related to lidocaine chemically.

On the basis of animal studies, which showed propitocaine to have an LD_{50} approximately 60% greater than that of lidocaine, and other animal studies, clinical investigation was begun. The drug was first used in human patients in Europe, where it was found to have longer duration of effect than lidocaine. Other studies indicated that with and without epinephrine, the new local anesthetic was equivalent to lidocaine in 0.5 to 2.0% concentration.

Patients aged 10 to 77 years participated in the present study. There were 186 women and 320 men. Twelve anesthetic procedures were used; 236 patients had a single caudal injection of the drug. Concentration used ranged from 1.5 to 3.0%; the total dose given varied from 225 to 1,860 mg. These

variations are consistent with clinical practices; however, the higher doses represent attempts at a repeated block after variable delay and continuous catheter technics. The large amounts should be given only by those who have wide clinical experience and facilities for emergency resuscitation.

Duration of anesthesia with 2 or 3% solutions ranged from 0 to more than 180 minutes. The anesthetic was adequate in 95.8% of the administrations; in only nine patients was there no anesthetic effect. Spreading of the anesthetic was apparently greater than that of lidocaine.

This evaluation is based on a patient sample too small to be definitive. Further study of the drug is warranted.

Drug Combinations — Uses, Dangers, and Fallacies

Jick, Hershel, and Chalmers, Thomas C.
Clin. Pharmacol. & Therap. 5:673-676, 1964

The use of more than one drug for the treatment of a single disease or symptom is rooted in the history of medicine. Multidrug therapy is hard to resist.

Perhaps indiscriminately prescribed in the past, use of drug combinations in a controlled fashion has been more carefully investigated recently. As a result of these studies, the validity of combination therapy has been established in many diseases. Those include tuberculosis, subacute bacterial endocarditis, hypertension, epilepsy, and fluid retention states. Multihormone therapy for birth control is well established.

On the most elementary level, different drugs may be prescribed to alleviate the multiple components of a patient's complex symptomatology. Thus tranquilizers and analeptics may be combined for the relief of tension headaches and myalgia. A more sophisticated approach may be based on physiologic or biochemical considerations. For example, treatment of hypertension was based on the premise that plasma volume, sympathetic discharge, and smooth muscle contractility were important causal factors. Drugs directed at two or more of these factors might result in an effective gain of blood pressure control, with lower doses of the drugs used in combination. This physiologic rationale proved sound.

Frequently, this approach to therapy, based on animal or *in vitro* observations, does not carry over to human beings. Under such circumstances, the usefulness of combinations must be determined by empirical methods in human trials.

The impetus to multidrug therapy has been provided in part by the realization that certain diseases respond well to drug combinations and in part by the appearance of tranquilizers, cortisone derivatives, and synthetic analgesics. These drugs are alleged to have a broad spectrum of effect, and the temptation to add one to established agents has not been resisted.

The use of fixed, single-dose combinations has receded from levels attained in the past. This is borne out by analysis of advertisements appearing in medical journals. The practice has disadvantages. The most obvious of these

is the impossibility of adjusting individual doses to the individual patient. The other disadvantage is more ephemeral: the psychological tendency among physicians to prescribe combinations, if this can be done with one prescription, on the assumption that extra ingredients might give added effect. This has serious defects: recent reports of renal damage associated with phenacetin, taken with aspirin, are a good example. Others can be cited.

There is also the problem of drug incompatibility. An example of this is the recent report of serious effects when monamine oxidase inhibitors and certain narcotics or sympathomimetic drugs are combined.

In the final analysis, combination therapy must be considered when single drugs are not optimally effective or when toxicity is high. But the combinations must be evaluated as thoroughly together as the components were evaluated singly.

Efficacy and Adverse Effects of Vasoconstrictors Used as Adjuncts in Regional Anesthesia

Stevenson, Arthur; Adriani, John, and Hyde, Edwin.
Anesthesia & Analgesia 43:495-500, 1964

The terms vasoconstrictor and vasopressor denote the same class of drugs. Generally, vasoconstrictor implies that vasomotion is confined to a local region; vasoconstriction is sought in order to retard absorption of another drug, for hemostasis, or for decongestion of mucous membranes. Vasopressor is used to designate the systemic responses of the drug. The response is characterized principally by an elevation of blood pressure.

Today the combination of epinephrine and a local anesthetic is used extensively for infiltration, intrathecal, peridural, and topical anesthesia. Vasoconstriction extends duration of the blockade and averts or attenuates the systemic effects of the local anesthetic due to high plasma levels.

Studies designed to compare the effectiveness of vasoconstrictors were carried out with patients who required repeated saddle or low spinal block anesthesia. The effectiveness of the drugs used, in declining order, was epinephrine, norepinephrine, pitressin, phenylephrine, ephedrine, methoxamine, mephentermine, and metaraminol. Only the first three drugs in this list, and an investigative drug, PLV-2, are really effective. Angrotensin was ineffective.

Vasoconstrictors alone had no local anesthetic effect, local anesthetics also have no demonstrable vasoconstricting action. Adverse local effects to vasoconstrictors have been reported. Clearly the drugs should not be used in the presence of circulatory impairment. Adverse systemic effects are the result of the use of excessive quantities. Patients with cardiovascular disease should be treated carefully with vasoconstrictors.

Form #8. General Consent Form

Date _____

I authorize Dr. _____ to perform such dental operations and administer/or have administered such anesthetics as found necessary to perform these dental operations as are advisable in the treatment of _____
(patient's name)

on _____
(date of operation)

Signed _____
(patient or person authorized to consent for patient)

New ADSA Members

Angelillo, Dr. John C.
Duke University Medical Center
Durham, North Carolina

Baer, Dr. Harry L.
144 No. Dithridge Street
Pittsburgh 13, Pennsylvania

Belcher, Dr. Hal B.
414 First National Bank Building
Welch, West Virginia

Black, Dr. Norman W.
417 Mobberly Avenue
Longview, Texas

Brett, Dr. Maurice R.
925 East Ingalls Avenue
Pascagoula, Mississippi

Brothers, Dr. Carl E.
1711 North Front Street
Harrisburg, Pennsylvania

Buck, Dr. Irvin F.
Vets Administration Building
Brooklyn, New York

Cater, Dr. Ralph W.
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Chubin, Dr. Myron
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Chicago, Illinois

Cree, Dr. Edward K.
Queens General Hospital
Jamaica, New York

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Dimas, Dr. Louis T.
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Lerman, Dr. Salvador
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McKean, Dr. Thomas W.
U. S. Naval Hospital
Great Lakes, Illinois

McNeill, Dr. Samuel J.
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Hyattsville, Maryland

Rice, Dr. Jack B.
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Seattle, Washington

Ross, Dr. Peter C.
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Smith, Dr. Vincent P.
245 North Potomac Street
Hagerstown, Maryland

Sojourner, Dr. Richard H.
Anes. Dept. Delaware Hosp.
501 West 14th Street
Wilmington, Delaware

Stern, Dr. Joel K.
64 West Main Street
Freehold, New Jersey

Sund, Dr. John A.
327-100 First Avenue Building
Rochester, Minnesota

Vaughn, Dr. Richard A.
5050 Joy Road, Suite 405
Detroit, Michigan

Wechsler, Dr. Stephen M.
Med. Arts Building Dental Wing
Endicott, New York

Zall, Dr. Benjamin
1 West 8th Street
Bayonne, New Jersey

Analgesia Society To Meet

The American Analgesia Society will meet at the Barbizon Plaza Hotel in New York City on Tuesday, May 11th. A pre-meeting dinner will take place at 6:30 p.m. and the scientific session will begin at 8:30 p.m. It will consist of the following three talks:

"The Pharmaco-logic of Analgesia" by Harold L. Hamburg.

"Specific Applications of Analgesia to Oral Rehabilitation" by Dr. Victor I. Sendax.

"Analgesia in Pedodontics with Emphasis on Conservative Treatment of the Exceptional Child" by Dr. Harold Diner.

Further information can be obtained from Dr. Philip E. Shipper, 9 West 67th Street, New York, New York 10023.

Society Section

New York Society To Meet on May 5

The New York State Dental Society of Anesthesiology will meet during the week of the World's Fair Meeting of the Dental Society of the State of New York, on May 5, to hear Dr. Harry Langa speak on Analgesia for Modern Dentistry. The meeting will take place in the Madison Suite of the New York Hilton Hotel at 8 p.m. There will be a free cocktail party after the meeting. For further details, contact Dr. Norman Snyder, 103-42 Lefferts Boulevard, Richmond Hill 19, N. Y.

California Meeting in San Francisco

The California State Dental Society of Anesthesiology met on April 5 at Del Webb's Townhouse in San Francisco to hear Dr. Howard Slatoff speak on Stereotyped Concepts and Human Values. Dr. Carter S. Hjelte, secretary-treasurer, reports that plans for the 1965-1966 year are in preparation.

General News

Dr. Gerald Timmons To Lead Dentist Campaign for AFDE

Dr. Gerald D. Timmons, retired dean of Temple University School of Dentistry and a past president of the American Dental Association, will head a national campaign to solicit funds from practicing dentists, dental hygienists, and dental assistants throughout the nation.

Dr. Timmons, who lives in Scottsdale, Ariz., has accepted the chairmanship of the American Fund for Dental Education's third annual dentists and dental personnel campaign which will open in May.

In accepting the post, Dr. Timmons said:

"To step up dental education, we must build a more impressive record of dental giving to dental education. If we are to expect gifts from others not closely allied with the profession, we must be in a position to report that dentists and their personnel are doing all they can to support dental education themselves.

"This year we will urge that each dentist and dental auxiliary contribute. Only the positive interest and active support of each dentist and his auxiliary help throughout the nation can help the Fund properly expand its important programs."

The ADA proclaimed May as "AFDE Month" in 1964 to honor the Fund as the national agency for collection and distribution of voluntary contributions supporting dental education.

AFDE president Dr. Raymond J. Nagle, New York, reported that last year the Fund received contributions from dentists and dental personnel which ranged from $5 to $100. He said that although the total returns from dentists tripled those received in the Fund's first campaign held in 1963, "far too few dentists were responding to the appeal."

Dr. Nagle said, "the Fund must have a far better showing this May to continue its vital support of the dental schools."

FDI To Meet in Vienna June 26 to July 3

The 53rd Annual Session of the Fédération Dentaire Internationale will take place at the Vienna Hofburg under the patronage of the Federal President of Austria from June 26 to July 3, 1965. Application forms and further information may be obtained from Dr. Obed Moen, 6 Main Street, Watertown, Wis.